

Claims

1. A compound 8 to 50 nucleobases in length targeted to a nucleic acid molecule encoding metalloproteinase 12 (MMP-12), **characterized in** that said compound specifically hybridises to and inhibits the translation of MMP-12 protein.
- 5 2. A compound according to claim 1, wherein the target sequence is SEQ ID NO. 1 or equivalent functional homologues thereof.
3. A compound according to claim 1, wherein the target sequence is SEQ ID NO. 2 or equivalent functional homologues thereof.
4. The compound according to claim 1, wherein said compound is an antisense
10 oligonucleotide complementary to the mRNA.
5. The compound according to claim 1, wherein the oligonucleotide is a DNA molecule.
6. The compound according to claim 1, wherein the oligonucleotide is a RNA molecule.
- 15 7. The compound according to claim 4, wherein the antisense oligonucleotide has a sequence selected from the group consisting of SEQ ID NO. 3 - 14.
8. The compound according to claim 4, wherein the oligonucleotide is RNAi comprising at least an 8 nucleotide portion of a sequence selected from the group of SEQ.ID.NO 3 - 14. and having a total length of no more than 25 nucleotides.
- 20 9. A compound 8 to 50 nucleobases in length targeted to a nucleic acid molecule encoding MMP-12, said compound being an antisense oligonucleotide which specifically hybridizes to and inhibits the translation of MMP-12 in a mammal, **characterized in** that the compound is chemically modified by substitution in a non-bridging oxygen atom of the antisense nucleic acid backbone with a moiety selected from the group consisting of
25 methane phosphate, methyl phosphate, and phosphorothioate.

10. The compound according to claim 9, wherein the substitution occurs at one or more nucleotides selected from the 3' end or the 5' end or both.
11. The compound according to claim 9, wherein the substitution occurs at one or more nucleotides at any position along the entire length of said oligonucleotide.
- 5 12. The compound according to any one of the preceding claims, wherein said compound is an antisense oligonucleotide composed of DNA or RNA or an analogue or mimic of DNA or RNA including but not restricted to the following: methylphosphonate, N3'->P5'-phosphoramidate, morpholino, peptide nucleic acid (PNA), locked nucleic acid (LNA), arabinosyl nucleic acid (ANA), fluoro-arabinosyl nucleic acid (FANA) methoxy-ethyl nucleic acid (MOE).
- 10 13. The compound according to claim 1, wherein said compound is an antisense oligonucleotide that is a homo or heteropolymer containing combinations of the above DNA or RNA or analogues or mimics of DNA or RNA.
14. The compound according to any one of claims 2 - 8, wherein in that said
15 oligonucleotide comprises at least one modified sugar moiety nucleobase.
15. The compound of claim 14, wherein the modified sugar moiety is a 2'-O-methoxyethyl sugar moiety.
16. A composition comprising the compound according to any one of the preceding claims and a pharmaceutically acceptable carrier or diluent.
- 20 17. The composition of claim 16, wherein said composition further comprises a colloidal dispersion system.
18. A method of inhibiting the translation of MMP-12 in cells or tissues, wherein said cells or tissues are contacted with the compound of any one of claims 1 - 15 thereby inhibiting the translation of MMP-12.
- 25 19. A method of inhibiting the translation of MMP-12 in cells or tissues, wherein said cells or tissues are contacted with the composition of any one of claims 16 - 17 thereby inhibiting the translation of MMP-12.

20. The method according to claim 18 or 19, wherein the inhibition of the MMP-12 expression suppresses a MMP-12 dependent process in a human subject.
21. The method according to claim 20, wherein the MMP-12 dependent process is one of inflammatory bowel disease, such as ulcerative colitis and Crohn's disease,
5 rheumatoid arthritis, psoriasis, emphysema and asthma.
22. A method of preventing, alleviating or treating a MMP-12 dependent disorder in a human patient, **characterized** in that MMP-12 expression is suppressed in one or more cells in said patient.
23. A method of preventing, alleviating or treating a MMP-12 dependent disorder in a
10 human patient, **characterized** in that the level of MMP-12 is suppressed in one or more cells in said patient.
24. The method according to claim 22 or 23, wherein said MMP-12 dependent disorder is one of inflammatory bowel disease, such as ulcerative colitis and Crohn's disease, rheumatoid arthritis, psoriasis, emphysema and asthma.
- 15 25. A recombinant nucleotide sequence comprising a compound according to any one of claim 1-15.
26. A recombinant expression vector comprising the recombinant nucleotide sequence according to claim 25.
27. The recombinant expression vector according to claim 26, wherein the vector is of
20 eukaryotic or prokaryotic origin.
28. A method of inhibiting the expression of MMP-12 in cells or tissues, wherein said cells or tissues is contacted *in vivo* or *in vitro* with the recombinant nucleotide sequence expressed by the recombinant vector according to claim 27.
29. A recombinant host cell produced by the method of claim 28.
- 25 30. A transgenic non-human animal, wherein said animal carries at least one sequence according to claim 7 functionally inserted in at least one cell.

31. The transgenic animal according to claim 30, wherein the at least one functionally inserted sequence is over-expressed.

32. A method of inhibiting the expression of MMP-12 in cells or tissues, wherein a composition according to claim 16 or 17 is administered to a human in a therapeutically effective dose together with a pharmaceutically acceptable carrier.

33. A method of diagnosing inflammatory bowel disease in a human subject, wherein the method comprises screening for the presence or absence of the expression of MMP-12 and the expression of MMP-12 is an indication of inflammatory bowel disease.
